

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1.-12. (Canceled)

13. (Currently Amended) An aqueous pharmaceutical composition comprising an antibody, or antigen-binding portion thereof, at a concentration between about 20 and about 130 mg/ml, a polyol, a surfactant, and a buffer system comprising at least one buffer selected from the group consisting of citrate and phosphate, with a pH of about 4 to about 8, in amounts sufficient to formulate the antibody for therapeutic use.

14. (Original) The composition of claim 13, wherein the polyol is mannitol and the surfactant is polysorbate 80.

15. (Original) The composition of claim 14, which contains about 5 to about 20 mg/ml of mannitol and about 0.1 to about 10 mg/ml of polysorbate 80.

16. (Currently Amended) The formulation of claim 13, wherein the which contains an antibody, or antigen-binding portion thereof, which binds human tumor necrosis factor alpha (TNF α) and is the antibody D2E7, or antigen binding portion thereof.

17. (Currently Amended) A liquid aqueous pharmaceutical formulation comprising
(a) about 20 to about 130 2 to about 150 mg/ml of antibody, or an antigen binding portion thereof,
(b) about 5 to about 20 mg/ml of mannitol,
(c) about 0.1 to about 10 0 to about 15 mg/ml of polysorbate 80 and
(d) a buffer system comprising at least one buffer selected from the group consisting of citrate and phosphate, with a pH of about 4 to about 8.

18. **(Original)** The formulation of claim 17, wherein the pH is selected from the group consisting of between about 4.5 to about 6.0, between about 4.8 about 5.5, and between about 5.0, and about 5.2.

19. **(Currently Amended)** The liquid aqueous pharmaceutical formulation of claim 17, which contains

(a) about 40 to about 100 ~~50~~ mg/ml of antibody, or antigen-binding portion thereof,

(b) about 7.5 to about 15 ~~42~~ mg/ml of mannitol, and

(c) about 0.5 to about 5 ~~4~~ mg/ml of polysorbate 80, and

(d) a buffer system comprising at least one buffer selected from the group consisting of citrate and phosphate with a pH of about 4 to about 8.

20. **(Currently Amended)** The formulation of claim 17, wherein the buffer system comprises

(a) about 1 to about 1.5 ~~4.3~~-mg/ml of citric acid,

(b) about 0.25 to about 0.5 ~~0.3~~ mg/ml of sodium citrate,

(c) about 1.25 to about 1.75 ~~4.5~~ mg/ml of disodium phosphate dihydrate,

(d) about 0.7 to about 1.1 ~~0.9~~-mg/ml of sodium dihydrogen phosphate dihydrate, and

(e) about 6.0-6.4 ~~6.2~~-mg/ml of sodium chloride.

21. **(Currently Amended)** The formulation of claim 19, wherein the antibody, or antigen-binding portion thereof, is directed to tumor necrosis factor alpha (TNF α).

22. **(Original)** The formulation of claim 19, wherein the antibody, or antigen-binding portion thereof, binds human tumor necrosis factor alpha (TNF α) and is the antibody D2E7 or an antigen binding portion thereof.

23. **(Original)** The formulation of claim 22, which is administered to a subject suffering from a disorder in which tumor necrosis factor alpha (TNF α) activity is detrimental such that TNF α activity in the subject is inhibited.

24. **(Currently Amended)** The liquid aqueous pharmaceutical formulation of claim 17, which contains

- (a) about 50 mg/ml of antibody, or antigen-binding portion thereof,
- (b) about 12 mg/ml of mannitol, and
- (c) about 1 mg/ml of polysorbate 80 polysorbate 80.

25. **(Currently Amended)** A stable pharmaceutical formulation comprising a human anti-Tumor Necrosis Factor alpha (TNF α) antibody, or antigen-binding fragment thereof, Adalimumab at a concentration of between about 20 2 and about 150 mg/ml, and a buffer system comprising citrate and phosphate mg/mL,

wherein said formulation has a pH of about 4 to about 8, and

wherein the antibody, or antigen-binding portion thereof, comprises a light chain variable region comprising a complementary determining region (CDR) 1 domain comprising the amino acid sequence set forth in SEQ ID NO:7; a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO:5; and a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO. 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7, or 8, or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8, and/or 9; and

comprises a heavy chain variable region comprising a CDR 1 domain comprising the amino acid sequence set forth in SEQ ID NO:8; a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO:6; and a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO. 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10, or 11, or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11, and/or 12.

26. **(New)** A liquid aqueous pharmaceutical formulation comprising

- (a) about 20 to about 130 of a human anti-Tumor Necrosis Factor alpha (TNF α) antibody, or antigen-binding portion thereof;
- (b) 5-20 mg/ml of mannitol,
- (c) 0.1-10 mg/ml of polysorbate-80, and

(d) a buffer system comprising citrate or phosphate, or a combination thereof, with a pH of 4 to 8,

wherein the antibody, or antigen-binding portion thereof, comprises a light chain variable region comprising a complementary determining region (CDR) 1 domain comprising the amino acid sequence set forth in SEQ ID NO:7; a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO:5; and a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO. 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7, or 8, or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8, and/or 9; and

comprises a heavy chain variable region comprising a CDR 1 domain comprising the amino acid sequence set forth in SEQ ID NO:8; a CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO:6; and a CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO. 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10, or 11, or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11, and/or 12.

27. **(New)** The formulation of any one of claims 21, 25, or 26, wherein the antibody, or antigen binding portion thereof, comprises a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1, and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

28. **(New)** The formulation of claim 25 or 26, wherein the antibody, or antigen binding portion thereof, is D2E7, or antigen-binding portion thereof.